intended to study metabolic changes in skeletal muscle biopsy specimens in patients with mild to moderate heart failure after myocardial infarction to evaluate the influence of ramipril treatment on these changes.

Methods: Biopsies were obtained from the Vastus muscle at baseline and after 6 months of treatment with ramipril or placebo. Biopsies were analysed for ATP, creatine, creatine phosphate, glycogen and lactate. Ejection fraction was evaluated by two dimensional echocardiography. Twenty-three male and 10 female patients, mean age 67 years (range 43–81 years), with symptoms of heart failure after myocardial infarction participated in this study. Eighteen men and 6 women mean age 65 years (range 54–75 years), with no history or clinical signs of heart disease admitted for minor surgery, were used as controls.

Results: Patients had mild to moderate left ventricular dysfunction, mean ejection fraction of 48%. We found a reduction in ATP 20% $p < 0.0001$, total creatine 13% $p < 0.0005$ and glycogen 15% $p < 0.05$ in patients compared to healthy controls. Six months treatment with ramipril didn't alter these changes.

Conclusions: Depletion of energy rich substrates ATP, creatinine and glycogen is seen in patients with mild to moderate heart failure early after myocardial infarction. Treatment with ramipril seems not to revert this depletion when developed.

1227 Cardiac Transplantation: Studies of Coronary Flow

Wednesday, April 1, 1998, 3:00 p.m.–5:00 p.m.
Georgia World Congress Center, West Exhibit Hall Level
Presentation Hour: 4:00 p.m.–5:00 p.m.

1227-56 Microvascular Endothelial Dysfunction Is Associated With Expression and Activation of Nitric Oxide Synthases and Endothelin Early After Cardiac Transplantation in Humans

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Background: Expression and Production of vasoactive mediators may contribute to endothelial dysfunction and graft atherosclerosis after heart transplantation (HTx). We investigated the relationship of inducible, constitutive nitric oxide synthases (iNOS, cNOS), endothelin (ET) and cytokines and microvascular endothelial dysfunction (ED) in 42 humans 37 ± 5 days after HTx.

Methods: Gene expression of iNOS, cNOS and ET was performed by RT-PCR. Coronary sinus (CS) and aortic plasma ET (fmol/ml) and nitrite (μM) were measured. Endothelium dependent vasomotion was assessed with Acetylcholine (ACh, 30 μg/min) by Doppler flowire. Exclusion criteria were acute infection or rejection episodes and presence of CAD.

Results: In 26.1% (n = 11) an impaired flow increase (1.65 ± ± 0.23) suggesting ED. In all patients (pts) iNOS, cNOS and ET expression was present. Transcardiac cytokine production was noted in nearly 60% of pts for IL-6, TNF-Rp2 and TNF-alpha. An increase in nitrite release was found (Aorta: 43.9 ± 3.7 vs CS: 52.8 ± 5.6, $p < 0.05$) suggesting transcardiac nitric oxide production. CS nitrite correlated with CS TNF-alpha levels ($r = 0.44$, $p < 0.05$). A transcardiac ET net extraction was found in patients with ED: (Aorta: 12.9 ± 0.57 vs CS: 9.8 ± 0.4, $p < 0.05$).

Conclusions: These findings provide evidence the microvascular endothelial function is impaired in 26% of pts in an early phase after HTx. Correlation between vasoactive mediators and pro-inflammatory cytokines suggest a chronic (smolder) immunologic process in the development of microvascular ED which may be an important therapeutic target in pts after HTx.

1227-57 The Effects of Acute Cellular Rejection on Intimal Thickening and Coronary Flow

T.L. Wolford, T.J. Donohue, L.A. Miller, R.G. Bach, E.A. Caracciolo, M.J. Kern, K. Riad. *Steven Kelly Saint Louis University, USA*

Transplant coronary arteriopathy (TCA) is postulated to develop secondary to chronic vascular immune responses. The effects of repeated episodes of acute cellular rejection on the subsequent development of TCA and on coronary flow reserve (CFR) have not been well studied. In 44 patients ≥1 year post-transplant the CFR was measured (Doppler guide wire and adenosine) in the LAD, CFX, and RCA. Intracoronary ultrasound (ICUS) was performed in the LAD or CFX of each patient and analyzed to assess average vessel mean intimal index and mean intimal thickness. An average biopsy score for the first 6 months post transplant was calculated using a numerical grading scale (0 = 0, 1A = 1, 1B = 1.5, 2 = 2, 3A = 3, 3B = 3.5) divided by the number of biopsies. The mean CFR and ICUS parameters were correlated with the average biopsy score using the non-parametric Spearman's rank correlation.

Results: Higher average biopsy grades in the first 6 months post transplant correlated with lower coronary flow reserves ($r = -0.34$, $p = 0.038$). There was no correlation between rejection history and any ICUS parameter.

Conclusion: The cumulative effect of early chronic acute cellular rejection results in late microvascular dysfunction as measured by a diminishment in CFR but has no correlation with the subsequent development of epicardial TCA.

1227-58 Intraindividual Variability of Coronary Flow Reserve in Heart Transplant Recipients With Angiographically Normal Coronary Arteries. A Study With Intracoronary Doppler and Ultrasound

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Background: Coronary flow reserve (CFR) is an important parameter of graft function after heart transplantation (Htx). In most reports on patients after Htx, CFR measurements performed in one of the epicardial vessels were considered representative for global graft function. The purpose of this study was to assess potential differences in CRF values between different coronary arteries.

Methods: We studied 57 patients (P, mean age 48 ± 13 years) with normal coronary angiography 38 ± 41 months after HTx using intracoronary Doppler (0.014 in. Doppler guide wire) and ultrasound (ICUS). CFR was determined after i.c. administration of 16 μg adenosine both in the left anterior descending artery (LAD) and in the circumflex artery (LCx). The extend of graft vasculopathy (TxCAD) was quantitated by ICUS (motorized pullback) using the mean intimal index of each vessel.

Results: CFR ranged from 1.1 to 5.7. CRF values showed no differences between LAD and LCx (3.1 ± 0.9 vs. 2.9 ± 0.6, NS). The correlation of flow parameters between both coronary arteries was good ($r = 0.74$, $p < 0.001$). However, the relative difference in CRF values between LAD and LCx ranged from 1% to 42% (mean, 17 ± 11%). In 17% of the P with normal CFR (> 2.5) in the LAD, reduced values (< 2.5) were in observed in the LCx. Mean intimal index in both vessels was comparable (16 ± 14% vs. 15 ± 15%).

Conclusion: In individual patients, coronary flow reserve measurements may show marked differences between LAD and LCx. These findings should be taken into account when data of CFR measurement obtained in one epicardial vessel are considered representative for global graft function.

1228 Atrial Tachycardia and Fibrillation

Wednesday, April 1, 1998, 3:00 p.m.–5:00 p.m.
Georgia World Congress Center, West Exhibit Hall Level
Presentation Hour: 4:00 p.m.–5:00 p.m.

1228-161 Electrophysiologic Remodeling of the Atrium in Patients With Atrial Fibrillation

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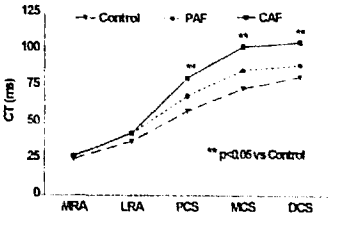
Previous studies have shown that sustained atrial fibrillation [AF] causes atrial electrophysiologic remodeling. Whether remodeling affects the atrium uniformly and consistently in patients [pts] with paroxysmal AF [PAF] and chronic AF [CAF] is unclear. We measured: 1) atrial conduction time [CT] at multiple sites in right atrium [RA] (mid & low) and left atrium [LA] (proximal, mid & distal coronary sinus [DCS]) during sinus rhythm; 2) effective refractory periods [ERPs] at high RA [HRA], low RA [LRA] and DCS at 400 & 600 ms drive cycle length (4 × threshold) in 11 pts (mean age:61 ± 15 yrs) with CAF (mean AF duration: 19 ± 6 mths) after successful transvenous defibrillation; 8 pts (mean age: 47 ± 14 yrs) with PAF and 10 controls (C) (mean age: 50 ± 12 yrs).



Results: No significant difference in RA CT was observed. CAF pts had significantly prolonged LA CT vs C. CAF pts had significant shortening of DCS ERPs and paradoxically prolonged LRA ERPs as compared with C. Both PAF and CAF pts had lost normal adaptation of ERPs at HRA & DCS, but was preserved in LRA.

ERPs	HRA	LRA	DCS
CAF 400	186	195	181
600	188	207*	182
PAF 400	186	183	209*
600	200	193*	217*
C 400	185	169*	201
600	193*	174*†	214*†

*p < 0.05 vs 400 †p < 0.05 vs CAF

Conclusions: 1) In CAF, electrophysiological abnormalities mainly occur in LA. 2) Electrophysiologic remodeling seen in pts with AF affects the atrium nonuniformly with shortening or prolongation of ERPs in different parts of atrium, which may increase the heterogeneity of atrial electrophysiological properties and contributes to perpetuation of AF. 3) PAF is associated with a modest prolongation of LA CT and maladaptation of ERPs in high RA and DCS, suggesting progressive atrial electrophysiologic remodeling.

1228-162 Biatrial High Density Mapping of Electrically Induced Atrial Fibrillation in Humans

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Background: High density electrical mapping of both atria during electrically induced atrial fibrillation (AF) in humans has not been previously reported.

Methods: Using a 2.4 × 2.2 cm symmetrical mapping plaque (528 unipolar electrodes, 1 mm interelectrode distance), detailed sequential epicardial mapping of the right atrium (RA) and the left atrium (LA) was performed in 5 patients (age 61 ± 10 yrs, LVEF 50 ± 6.4%) undergoing CABG surgery. AF was induced by rapid atrial burst pacing. Recordings were obtained from both the RAA and LAA.

Results: A total of 18 seconds of activation patterns were analyzed. The mean cycle length during AF was 188 ± 58 ms (range 125–288 ms) in the RA and 204 ± 36 ms (range 148–268 ms) in the LA. In 4/5 patients, LA activation patterns were more complex with a higher incidence of fragmentation. Although complete reentry was not visualized, long lines of functional conduction block were more frequent in the RA with propagation of the wavefronts along the site of block. Non-repetitive focal epicardial activations were twice as common on the LA compared to the RA. Conduction velocities were not significantly different (RA 52.3 ± 3.4 cm/s vs. LA 55.7 ± 5.2 cm/s, p = 0.08). Electrical inactivity over the mapping plaque was greater during LA recordings (4.1 s) compared to the RA (2.7 s).

Conclusions: In electrically induced AF, LA activation patterns appeared to be more complex with a higher incidence of focal epicardial activations and wavefront fragmentation compared to the RA despite a greater mean cycle length and longer periods of electrical silence.

1228-163 Cycle Length Dependence of Action Potential Duration and Dispersion in the Human Atrium

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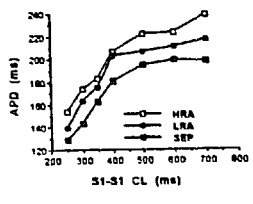
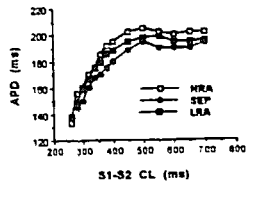
Background: The cycle length (CL) dependence of action potential duration (APD) has been well characterized for the human ventricle by monophasic action potential (MAP) recordings but only minimal data are available on CL dependence of *atrial* APD in the human heart.

Methods: In 7 patients, MAPs were recorded simultaneously from high (HRA), low (LRA) and septum (Sep.) right atrial sites during both steady-state (SS) pacing from 700 to 250 ms and extrastimulus (ES) pacing from 700 ms to refractoriness at 600 ms basic CL.

Results: Steady-state APD at 600 ms CL was longer (242 ± 42 ms) at HRA than Sep (211 ± 35 ms, p < 0.05), with LRA in between. This dispersion decreased towards shorter CL. ES-curves also were dispersed at long CL (HRA 200 ± 27 vs. LRA 179 ± 25 ms at 600 ms, p < 0.05). Examples for SS (left) and ES (right):





Conclusions: 1) SS and ES APD show CL dependence similar to that reported in ventricular studies; 2) APD varies from site to site in the human right atrium, especially at longer CL; 3) CL and site dependence of atrial APD may be important for understanding pacing related efforts to prevent atrial fibrillation.

1228-164 Three-dimensional Computer-assisted Animation of Atrial Tachyarrhythmias Recorded With a 64-Polar Basket Catheter

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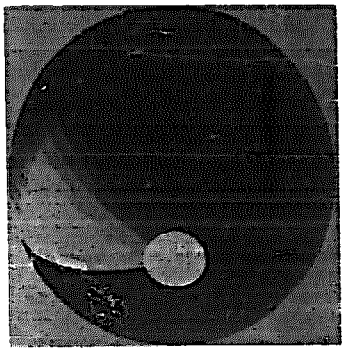
The use of a 64-polar basket catheter (B) (Constellation catheter, EPT) allows multipolar threedimensional recording of atrial tachyarrhythmias in the clinical electrophysiologic laboratory. Thus the intraatrial activation sequence can be demonstrated.

Methods: We developed a software for the automatic analysis of the activation sequence. The B was used in the right atrium in 36 pts with atrial tachyarrhythmias: inappropriate sinus tachycardia in 4 pts, common type atrial flutter in 18 pts, uncommon atrial flutter in 4 pts and focal atrial tachycardia in 10 pts. The signals were recorded with a BARD EP-Lab system and transfered to an office personal computer. After evaluation of the 56 different bipolar leads the activation sequence can be visualized as a projected globe (Figure: common type atrial flutter, basal exit). The activation sequence is coded by changing colors.

Results: In all 22 pts with a reentry mechanism the reentry was located in the right atrium and could be demonstrated as a return of the activation to the exit area. In all but 2 patients with a focal atrial tachycardia, where the focus was located in the left atrium, the focal mechanism was demonstrated.



Conclusion: The animation of atrial tachyarrhythmias, recorded with a basket catheter, allows a simple instantaneous differentiation of the underlying mechanism in most of the patients.

1228-165 Atrial Conduction After Intracardiac Defibrillation of Atrial Fibrillation: Correlation to Relapse

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Intraatrial defibrillation of atrial fibrillation (AF) is a highly effective method. However, a lot of successfully treated patients will have relapses despite antiarrhythmic drug treatment. The aim of the study was to find markers for recurrences of AF.

Patients and Methods: The study consists of 15 patients (8 male, 7 female, age ranged between 31 and 70 years) with persistent AF after several ineffective external countershocks. LVEF ranged between 44 and 62, left atrial diameters between 38 and 50 mm. All patients were successfully converted to sinus rhythm using biphasic shocks between 3 and 25 J through two coil electrodes between high right atrium (HRA) and coronary sinus (CS). Interatrial conduction was measured 10 min after shock using extrastimulus technique at HRA and SC beginning 10 min after the shock.

Results: There were 2 early and 6 late relapses despite treatment with flecainide (n = 4) or propafenone (n = 4). Interatrial conduction is shown in the table:

	HRA-CS	HRA-CS$_{max}$	CS-HRA	CS-HRA$_{max}$
relapse	168 ± 39	186 ± 46	189 ± 29	189 ± 16
no relapse	131 ± 36	177 ± 28	155 ± 25	183 ± 27

Conclusions: Prolonged and decremental interatrial conduction is a common observation in persistent, drug-and external defibrillation refractory atrial